POLICY AND COMMUNICATIONS BULLETIN
THE CLINICAL CENTER

Medical Administrative Series

M01-2 2 November 2001

MANUAL TRANSMITTAL SHEET

SUBJECT: Procurement and Use of Human Biological Materials for Research

1. Explanation of Material Transmitted: This issuance transmits the policy of the Clinical Center on the collection and use of human tissue samples in research. This policy was approved by the Medical Executive Committee on 4 September 2001.

2. Material Superseded: None

3. Filing Instructions: Informed Consent

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Distribution:

Physicians, Dentists and Other Practitioners Participating in Patient Care

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SUBJECT: Procurement and Use of Human Biological Materials for Research

PURPOSE

- To ensure that procurement and use of human biological materials for research occurs only after review and approval by an NIH Institutional Review Board (IRB), or a determination of exemption issued by the NIH Office of Human Subjects Research (OHSR).
- To protect investigators' access to human biologic materials collected under protocols, while providing access of others to the archival CC specimen collection (THE ARCHIVE) maintained by the National Cancer Institute/Center for Cancer Research/Laboratory of Pathology (LP).
- To provide mechanisms for documenting and tracking the acquisition of human biologic materials by investigators (rather than the pathology department).

DEFINITIONS

- Human biologic materials, for the purpose of this policy, include all tissues and fluids obtained from living individuals, with the exception of blood. (The collection of blood is addressed under M95-9, "Guidelines for Blood Drawn for Research Purposes in the Clinical Center.")

- The National Cancer Institute/Center for Cancer Research/Laboratory of Pathology (LP) is legally accountable for diagnostic human biological materials obtained in the CC. It must safeguard proof of diagnoses based on these materials and by law must retain and protect sufficient archived materials (e.g., slides, blocks) for diagnostic purposes.

POLICY

1) Human biologic materials may be used for research only after obtaining IRB approval, or an exemption from OHSR. IRB approval includes review of the protocol, written informed consent (or waiver of consent), and need for pathologic review of the specimens.

   a) All protocols and informed consents will address the issue of human biologic materials acquisition and research use as a mandatory inclusion item, including discussion of whether the human biologic materials will be reviewed by a pathologist. In accord with the Federal Regulations for the Protection of Human Subjects, the IRB has the authority to waive the requirement for research subject consent for the research use of human biological materials in certain circumstances. This authority is generally exercised for retrospective or anonymized studies. Investigators are advised to consult the IRB for advice on this matter.

   b) All human biologic materials must have clinical pathologic review unless the IRB approves a waiver of this pathologic review for specimens obtained for research. For example, biopsies of skin blisters that were produced for purposes of research may not require pathology review for clinical purposes. However, while not required for clinical care in this setting, pathologic review may provide useful research endpoints. When human biologic material is collected for research, the consent form must indicate whether human biologic materials will undergo formal pathology review.

   c) Investigators may use an IRB-endorsed generic language that will require IRB approval in the context of the specific protocol.

2) Investigators and those who acquire human biologic materials will document the protocol intent to obtain human biologic materials and the eventual acquisition of the human biologic material(s).

   a) The 1195 form shall document the intent to collect human biologic material for research, either as “none” “blood” or “other biologic material.” This information will be entered into the protocol services database and will be available to the LP to

track protocols that involve collection of non-blood biologic material.

b) The "Research Tissue Procurement & Transfer Documentation" medical record form (appendix A) with instructions (appendix B) will be used to provide a record of transfer of human biologic materials from the point of acquisition to a site other than the Laboratory of Pathology. This record will reduce the chance that human biologic material is procured for an investigator without IRB approval, or that human biologic material will be acquired only for research when a diagnostic specimen also is necessary.

c) Individuals performing procedures to remove human biologic materials other than blood must document this procedure in the medical record.

d) Transfer of identifiable tissue to non-NIH investigators will be documented in the medical record and also will require patient signature for materials release.

3) The NCI Laboratory of Pathology (LP) will maintain in the ARCHIVE sufficient specimen for diagnostic purposes and will prospectively protect specimens originally obtained for research purposes.

a) Guidelines in the LP will protect patient diagnostic material and protocol-specific archived material through a standardized application process through which an investigator requests human biological materials (see below).

b) Archival Clinical Center specimen collection materials cannot be released unless sufficient diagnostic material is maintained. Specimens prospectively collected for particular protocols will be protected from non-protocol specific research.

4) The NCI Laboratory of Pathology (LP) will facilitate acquisition of human biologic materials from THE ARCHIVE.

a) To obtain specimens, intramural and extramural investigators will submit a "Request for Human Biologic Materials for Research Purposes" form that identifies the Principal Investigator, resource needs (service, tissue, slide preparation,

and anticipated methodology), and protocol approval, waiver or consent, or OHSR exemption.

b) LP will monitor turn-around-time for these requests to assess the quality of its service.

PROCEDURES

1) Responsibilities of the Intramural Principal Investigator and Research Team

a) When samples are collected, protocols must address human biologic materials acquisition in the body of the protocol; those that acquire human biologic materials must address this in the consent. All current protocols must be amended no later than the time of continuing review, to address items above. Investigators may use an IRB-endorsed generic language that will require approval in context by the IRB as per review requirements. The Principal Investigator is responsible for indicating on the protocol 1195 form whether human biologic materials will be obtained.

b) The research team will complete the "Research Tissue Procurement & Transfer Documentation" form and place it in the medical record.

c) To obtain archival specimens, investigators will submit the form "Intramural Request for Human Biologic Materials for Research Purposes" (appendix C) to the Laboratory of Pathology. The instructions for completing the form are outlined in an accompanying memo (appendix D). The form includes information about the research and the resource that is requested. This description is intended to allow a cross-check of whether the requested resource will work in the intended experiments—for example a plan to use PCR to amplify mRNA might not work well with paraffin sections.

2) Responsibilities of the IRB

a) The IRB will consider this policy when reviewing all new and continuing protocols.

3) Responsibilities of the Protocol Coordination Service Center

a) The Protocol Coordination Service Center will enter information about collection of human biologic materials into the protocol database and will provide this to the Laboratory of Pathology upon request.

4) Responsibilities of the individual or team who procures the human biologic materials

a) The individual or team who procures the human biologic materials will complete the "Research Tissue Procurement & Transfer Documentation" form, noting the type of tissue and amount taken, and asking the person who picks up the tissue to sign the form before releasing the human biologic materials.

b) Documentation of a procedure in the medical record must include information about the type of procedure performed, the human biologic materials (tissue) removed, and any complications. Ideally, this note should mention the disposition of the human biologic materials (tissue) and the protocol for which the human biologic materials (tissue) is acquired. When this is not feasible—for example an interventional radiologist is performing a biopsy for a protocol patient—the "Research Tissue Procurement & Transfer Documentation" form will provide this information.

5) Responsibilities of the Medical Record Department

a) The Medical Record Department will distribute the copies of the "Research Tissue Procurement & Transfer Documentation." A copy will remain in the medical record, with additional copies distributed to the Laboratory of Pathology and the Principal Investigator.

6) Responsibilities of the Laboratory of Pathology (LP)

a) The LP will follow standard operating procedures (SOP, full document available upon request) including guidelines for the protection of clinical material and archived material obtained for research. The SOP maintains accountability and protection of patient diagnostic material through a standardized application process through which an investigator requests human biological materials as noted elsewhere in this policy.

The Protocol Services database will be available to the LP to track protocols that involve collection of non-blood biologic material for research. In turn, that information will be used to gate the access of non-protocol investigators to THE ARCHIVE.

b) The LP will process requests for acquisition of human biologic materials from THE ARCHIVE as a service, according to the standard operating procedure discussed above (SOP, full document available upon request). The SOP assures that the LP operates within compliance of the legal and proper ethical authority to release archival biological materials or to divide fresh human biologic materials to satisfy research and clinical diagnostic needs. The LP will provide consultation about collaborative and non-collaborative proposals, but apart from this, will not review the proposed science or prioritize the requests by their perceived scientific merit.

c) Materials cannot be released from the archival Clinical Center specimen collection unless sufficient diagnostic material is maintained. If the requested material is in danger of being exhausted, the Pathologist and original Principal Investigator (PI), when applicable, must be consulted to determine if the request can be fulfilled.

d) LP will use a database of the requests to monitor turn-around-time and obtain internal quality control information. The attending staff of the Laboratory of Pathology will review applications. Incomplete applications are returned to the investigator. If there is a perceived problem with the proposed research, the LP reviewer will discuss the issues and provide a consultation to the research team about the proposed use. The LP will process the original request if the investigator does not decide to amend it. After approval, the appropriate service will fulfill the request. The Laboratory of Pathology is responsible for anonymizing the material if requested, and for protecting limited material (see above). Any interim documentation created in organizing the request for anonymized resources is destroyed at the time of releasing the material. Recuts will be billed to the CAN of the requesting Investigator.

e) Non-NIH investigators who request archival NIH human biologic materials will receive a letter (appendix E) from the

Laboratory of Pathology that explains the acquisition and billing process and asks the investigator to complete a "Extramural Request for Human Biologic Materials for Research Purposes" form (appendix F).

f) The Laboratory of Pathology will document transfer of identifiable human biologic materials to non-NIH investigators in the medical record by a copy of the "Request for Human Biologic Materials for Research Purposes" form and also will require patient signature for materials release.

g) Requests for tissue for research from extramural investigators require approval by the PI of the protocol under which the tissue was collected, if the sample was collected for research. The institute Clinical Director should review the request if the PI is unavailable.

MEDICAL RECORD	Request for Human Biological Materials Tissue Procurement & Transfer Form

INSTRUCTIONS:

- Complete one form for each recipient of research samples.
- Copy should be distributed at time of tissue transfer to Laboratory of Pathology, NCI, 10/2N212.

PART A: REQUEST & CERTIFICATION

(Completed by Principal/Associate Investigator)

Tissue will not be released unless Part A is complete and signed

Investigator Requesting Samples (print legibly):			Institute:	Branch:
Building:	Room:	Phone:	Page:	Date of Request:

Specimens Removed By This Procedure Will Be Acquired For (check one):

☐ Research Use Only ☐ Diagnostic and Research Purposes

Provide IRB Protocol Number:	Physician Performing Procedure:

Protocol Designated Research Sample and Recipient (Phone #/Pager):

I certify that the IRB approval covers both the protocol and patient-executed consent, and the research proposed is specified within the approved protocol and consent:

Signature of PI/AI of the Specified Protocol Date

PART B: DESCRIPTION OF RESEARCH MATERIALS

(Completed by Person Describing and Releasing Material/Tissue)

Tissue Acquired:

Quantity and measurements (dimensions or volume - cm, ml):

Name/Signature of Person Describing and Releasing Material/Tissue:

(print legibly) Signature Date

PART C: DESCRIPTION OF TRANSFER

(Completed by Person Picking Up Research Material)

Picked Up For: Phone/Page:

Name/Signature of Person Picking Up Material:

(print legibly) Signature Date

Patient Identification **APPENDIX A**	Request for Human Biological Materials Tissue Procurement & Transfer Form NIH-2803-1 (9-01) P.A. 09-25-0099 File in Section 4: Authorization

REQUEST FOR HUMAN BIOLOGICAL MATERIALS
TISSUE PROCUREMENT & TRANSFER FORM
(INSTRUCTIONS)

Note: This form is used when tissue is obtained for research. Do not use this form if materials are only obtained for pathology lab (NCI/CCR/LP) for clinical diagnostic purposes.

PART A: REQUEST & CERTIFICATION BY PRINCIPAL INVESTIGATOR
All information in part A must be completed prior to procurement of biological materials (tissues, fluids, etc) for research purposes.

1. Complete the patient identification information (Last name, First name, Middle initial, NIH Medical Record #) located in the lower left hand corner of the form.
2. Print the name of the principal investigator requiring tissue procurement and transfer of linked human biological materials for research purposes.
3. Complete the information principal investigator or associate investigator
   a. Institute/Branch of the PI
   b. Building/room number
   c. Phone and pager of the PI
4. Indicate date of request
5. Indicate whether the material is for
   a. Research use only (will not receive pathology review)
   b. Diagnostic purposes and research purposes (Laboratory of Pathology can be involved in the division of the material, when needed)
6. Provide the IRB Protocol # for this request.
7. Provide the name of the physician performing the procedure (person responsible for collecting the material (e.g., surgeon's name)
8. List the research material and the recipient of the material designated in the IRB approved protocol.
9. Obtain the signature of the Principal Investigator/Associate Investigator and date to certify the request.

PART B: DESCRIPTION OF RESEARCH MATERIALS
Part B is to be completed at the time of description and transfer of biological materials.

1. Describe tissue acquired (organ, left vs. right, anterior vs. posterior, etc where appropriate). ***Example: Pelvic lymph node, left***
2. Describe quantity and measurements (dimensions or volume –cm, ml). ***Example: Single pass, 1 ml.***
3. Record name of person describing and releasing material after procurement (e.g., pathologist, surgeon, nurse).
4. The person describing and releasing material must print name and sign form.

PART C: DESCRIPTION OF TRANSFER
Part C is to be completed at the time of description and transfer of biological materials.

1. Verify the name of the designated recipient in part A. Write in the name of the person the material is being picked up for.
2. The person picking up the material must print name and sign form and distribute the forms as follows:
   a. Send Top copy to Medical Records
   b. Second copy may be delivered to LP with diagnostic specimen or mailed to 10/2N212
   c. Retain the third copy for the research team.

APPENDIX B

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
National Institutes of Health
Bethesda, Maryland 20892
http://www.nih.gov

NCI LABORATORY OF PATHOLOGY
INTRAMURAL REQUEST FOR HUMAN BIOLOGICAL MATERIALS FOR RESEARCH PURPOSES

PRINCIPAL INVESTIGATOR INFORMATION

Principal Investigator (please print name legibly): _____
Institute: _____ **Branch:** _____**Building:** _____ **Room:** _____
Phone: _____ **Page:** _____ **Fax:** _____
E-mail: _____
Alternate Contact Information: _____
Alternate Phone: _____ **Page:** _____ **Fax:** _____
E-mail: _____
CAN number: _____

DESCRIPTION OF RESOURCE NEEDS

Type (must check) __ Linked (identifiable) __Anonymized __ Autopsy __Deceased
Tissue source requested: _____
__ Normal tissue
__ Abnormal tissue. Indicate key diagnostic terminology for database search.
Service: __ Autopsy __ Cytogenetics __ Cytopathology __ Flow cytometry
__ Hematopathology __ Immunohistochemistry __ Laser capture microdissection
__ Molecular diagnostics __ Surgical Pathology __ Other (specify): _____
Recuts: __ Recuts only (please attach list with patient name, NIH patient number, path number, block #)
__ Recuts with pathology review (attach list)
Tissue Type (circle all that apply): Fresh Frozen Paraffin Autopsy Cytology Other:_____
Circle recut slide type : Regular/untreated Gelatin Poly-L-Lysine Silanated Other/specify: _____
# of slide recuts: _____ ___ **check if recuts should be made using Rnase precautions.**
Other: _____
NOTE: Materials cannot be released unless sufficient diagnostic material is available for NIH archives.

INTENDED USE & METHODOLOGY (Attach additional pages if necessary)
Please include a list of any special requirements or exclusions, and include and expiration date of request if applicable.

OHSR EXEMPTION FORM or IRB APPROVAL NUMBER MUST BE PROVIDED

Attach OHSR Exemption Form or provide IRB Protocol #: _____
Note: An OHSR exemption is not required for Autopsy material. For release of material from non-living patients, please attach certification or proof that the patient has expired.

CERTIFICATION BY PRINCIPAL INVESTIGATOR

The approval provided covers both the protocol and patient-executed consent, and the research proposed is specified within the approved protocol and consent or IRB waiver of consent.
Signature of Principal Investigator of the specified protocol or waiver:

X _____**Date:** _____

***** INCOMPLETE FORMS WILL BE RETURNED TO PRINCIPAL INVESTIGATOR *****

For more information contact: Kevin Nellis, MT(ASCP), Clinical Lab Manager
(301) 594-9532 or NIH page 104-4613 or e-mail: nellisk@mail.nih.gov
Return form and attachments to: Laboratory of Pathology, Tissue Resource Committee
10 Center Drive, Room 10/22N212
Attn: Ms. Susan Gantz (gantzs@pop.nci.nih.gov)

APPENDIX C

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

National Institutes of Health
Bethesda, Maryland 20892
http://www.nih.gov

MEMORANDUM

To: Principal Investigator

From: NCI/CCR/Laboratory of Pathology
Tissue Resource Committee

Subject: Request for Human Biological Materials for Research

Thank you for your inquiry into Laboratory of Pathology for Human Biological Materials. Please fill out the attached request form. Your proposed experiment must be covered either by an existing IRB-approved protocol or exemption from the requirement for IRB review. You can contact the Office of Human Subjects Research (OHSR) for the exemption form or refer to web site: http://ohsr.od.nih.gov/

Biological material from autopsy cases or deceased patients does not require OHSR exemption or IRB approval. Release of biological material from deceased patients without an OHSR exemption requires certification or proof that the patient has expired.

Where necessary include information on IRB approval or exemption, protocol requirements, and patient name, CC number, pathology number, and block number if known. Support requests should be submitted to Mrs. Susan Gantz, Bldg 10, Room 2N212. Requests will be reviewed by the LP Tissue Resource Committee and forwarded to the Laboratory of Pathology Service Chief as quickly as possible.

Materials cannot be released unless sufficient diagnostic material is available for NIH archives. For those requests where adequate material is remaining, upon receipt of a completed form, the NCI Laboratory of Pathology, Histology section will oversee the preparation of the material. If a request cannot be accommodated based on the workload, it will be sent out to a reference laboratory chosen by NCI/LP at the requestor's expense. Current outside laboratory costs run from $2.95 per untreated, unstained slide to $3.35 per gelatin, lysine, or silanated slides and $7.35 per hematoxylin and eosin stained slides. Please include your CAN number to cover the cost of such request.

APPENDIX D

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

http://www.nih.gov

DHHS/NIH/NCI/DCS/LP
9000 Rockville Pike
Bethesda, Maryland 20892
Bldg 10 Rm 2N212, MSC 1516
Attn: Susan Gantz

October 9, 2001

<Type Investigator Name Here>

<Type Investigator Address Here>
<Type Investigator Address Here>
<Type Investigator Address Here>
<Type Investigator Address Here>

Subject: Request for human biological materials for research purposes

Dear Dr. <Type Investigator Name Here>:

Thank you for your inquiry about the National Cancer Institute Laboratory of Pathology (LP) Support Services. The NCI/LP Tissue Resource Committee (TRC) will evaluate requests as quickly as possible. All requests for paraffin block recuts without pathologic review will receive expedited review.

To obtain material, you must have an IRB approved protocol and consent for this acquisition. The patient's (or Guardian's) authorization for release of the sample is also required. The principal investigator must certify the research use of the requested human biological material will be in accordance with the IRB's determinations or that use has been determined to be exempt for IRB review and approval. This form will be added to the patient's medical record at NIH, even if the request is incomplete or denied.

It is the responsibility of the requestor to obtain the appropriate approval before requesting resources through NIH. LP is responsible and accountable by law for the use and protection of patient materials that are in its archive. By law, LP is accountable for patient materials and proof of diagnosis, (e.g., slides, blocks). If the requested material is in danger of being exhausted, the pathologist and the NIH PI under whose protocol the sample was originally collected must be consulted to determine if the request can be fulfilled. The TRC may question the technical approach of any request and may contact the requestor for additional information to justify or modify the request

Materials will not be released unless sufficient diagnostic material is available for NIH archives. For those requests where adequate material is remaining, upon receipt of a completed form, the NCI Laboratory of Pathology, Histology section will oversee the preparation of the material. It will be sent out to a reference laboratory chosen by NCI/LP at the requestor's expense. Current costs run from $2.95 per untreated, unstained slide to $3.35 per gelatin, lysine, or silanated slides and $7.35 per hematoxylin and eosin stained slides. Please provide billing information on the request form so that the reference lab may bill you for the service. Shipping will be billed to your Fed Ex account on your request or you may specify alternate shipping arrangements.

Respectfully,

Tissue Resource Committee

Enclosure (1)

APPENDIX E

MEDICAL RECORD	Extramural Request for Human Biological Materials For Research Purposes

PRINCIPAL INVESTIGATOR INFORMATION

Extramural Principal Investigator (print legibly)	Institution
Address	Phone: E-mail:

Billing Information for Recuts/Restains: _____

_____

(Reference Lab will bill requestor for work requiring recuts or restains)

Material will be shipped to above address unless otherwise specified. Indicate preferred shipping company and billing account number: _____

DESCRIPTION OF RESOURCE NEEDS

Tissue Source Requested:	Recuts:
☐ Normal Tissue ☐ Abnormal Tissue (indicate key diagnostic terminology for database search): _____	☐ Recuts Number of Slides: _____ ☐ Pathology Review ☐ RNase Precautions ☐ Other (specify): _____
Tissue Type (check all that apply):	Recut Slide Type (check):
☐ Paraffin ☐ Cytology ☐ Autopsy ☐ Other (specify): _____	☐ Regular/Untreated ☐ Poly-L-Lysine ☐ Gelatin ☐ Silanated ☐ Other (specify): _____

NOTE: Materials cannot be released unless sufficient material is retained for clinical diagnostic purposes.

Patient Name	NIH Medical Record Number	Patient Date of Birth
NIH Attending Physician (if known)	Date of Surgery/Specimen Collection	NIH Block Number(s) (if known)
Title of Your Protocol:		Date of Current Approval by Your IRB

Permission is hereby granted to the National Institutes of Health to release the materials requested herein and to obtain copies of pathology reports pertaining to the material to the individual/organization as identified above. (Note: submission of this form authorizes the release of materials and information specified within one year from date of signature.)

Patient (or Guardian) Signature _____ Date _____

CERTIFICATION BY EXTRAMURAL PRINCIPAL INVESTIGATOR

I certify that the research use of the requested human biological material will be in accordance with the IRB approved protocol and consent referenced above.

Signature of Extramural Principal Investigator _____ **Date** _____

APPROVAL BY INTRAMURAL PRINCIPAL INVESTIGATOR/CLINICAL DIRECTOR

☐ Approve ☐ Disapprove Date: _____

Signature: _____ Title: _____

FOR INTERNAL USE ONLY BY NCI, LABORATORY OF PATHOLOGY:

Date Received: _____ Outcome: _____ Signature: _____

Patient Identification **APPENDIX F**	Extramural Request for Human Biological Materials For Research Purposes NIH-2803-2 (9-01) P.A. 09-25-0099 File in Section 4: Authorization